

### ABSTRACT OF THE DISCLOSURE

Disclosed are improved methods of treating individuals with Alzheimer's disease (AD) as well as methods to diagnose AD in an individual. Also included are compounds and methods of identifying compounds to treat AD. The present invention also discloses methods for decreasing the phosphorylation of amyloid precursor protein (APP), including inhibiting phosphorylation of amino acid residue tyrosine 668 of APP and for reducing cleavage of APP. The present invention further discloses transgenic (Tg), non-human animals and cells expressing a p25 transgene that are models of neurodegenerative diseases. Embodiments of the present invention are directed to methods wherein the Tg animals and Tg cells of the invention are used to screen for modulators of neurodegenerative disorders. The Tg animals and cells of the present invention are useful for elucidating the mechanisms of neurodegenerative disorders.